Stone

May 29, 1961

Dear Bill:

As you might have suspected, I sent you the brochure on the Syntex Institute out of more than casual interest. Having gone a bit further into a proposal with the company directors, it may be appropriate to bring it up with you.

You should be able to get a fair impression of the Institute from the announcement, and from the people already lined up for it. The labs are now all but finished, and should be fully occupied by the end of the month. As you can judge there will be a concentration of interest on the chemistry and biochemistry of nucleic acids, and I think the team now getting under way should do a splendid job in this area. This is strictly an academic research program, and there is no forecasting just what return it may be able to make in the foreseeable future from the standpoint either of any useful drug products or any financial return to the company.

I think that Syntex made a fine move by establishing the Institute, but I do not feel that it should stop there in its biological research program. Its principal research activity until now has been in the chemistry of steroids, and it has done a remarkable job there; it has done almost nothing on their biology, relying on its outside contacts, e.g., Dorfman, and other drug house labs. for routine evaluation. I feel that they should set up their own biological research program, one which would be closely affiliated with the Institute for Molecular Biology, and whose orientation would fall somewhere in between the completely basic one of the Institute, and the routine aspects of product screening and evaluation that can be handled elsewhere. In particular, it seems to me that there is a real prospect that a concented attack could be made on the practical solution of the homograft problem through an understanding of the action of steroids on the immune reaction, and through the intelligent choice of existing or planned compounds.

W. Stone

In any case, I am planning to propose to Syntex that they establish at least a Department of Cell Biology within the SIMB, or perhaps even a parallel Institute of Cell Biology, that would be charged with the effort to achieve a practical solution to the homograft problem. This should entail a fairly broad program, including further basic research on histoincompatibility itself (viz. along lines like the work that you or Nossal have been doing), and on the design and validation of evaluation procedures that could give better insight into the practical usefulness of steroid, radiation, and chemotherapeutic (e.g. sytotoxic drugs) measures. Briefly, the purpose of the Institute would be to accelerate the actual solution of the problem, even if this solution is not altogether a completely satisfactory one at first, as it can hardly be if it is not based on a thorough understanding of the biological mechanism. On the likelihood that cortical steroid analogues are likely to play a significant role in such a solution, I think it possible that Syntex might be willing to underwrite a fairly extensive program. Many medical people are also impatient of the current pace and are doing overly ceurageous experiments that ought to be better validated by animal experiments first!

The present situation is that Syntex would certainly go for a modest program in this area, comparable say to an additional laboratory in the SIMB, and this is parhaps the way it will end up for the time being. However, I would like to try to make a case for a more ambitious one, that from the start would make a broader attack, and including short range model tests of prospective agents, as well as longer range work on cellular immunology. If this scheme works out, it would involve setting up another lab. about comparable to the present Molecular Biology Institute, but organized a little differently -- it would have a more senior director with actual responsibility for the whole program, and two or three research associates under his supervision. (At the SIMB, John Zderic is "director of laboratories", which is comparable to a department chairman, the research program being quite decentralized.)

I don't know how this is going to work out with Syntex, as it would involve a quite substantial further investment. I do think the transplantation field does need some more push along these lines (to complement the more strictly academic work at the universities), and people that Hal Holman here are quite impatient for such results. There are many other aspects, mainly very favorable that would be hard to summarize in a letter.

A crucial element is finding the right person to set up the laboratory, and I would not urge the program on Syntex until I at least had someone in mind as a possibility for it. It would be premature to suggest anything like a definite commitment on either side, but I would like to ask you whether you could consider the job yourself. Carl Djerassi is attending a director's meeting in Mexico in two weeks, and if I had some encouragement from you, I would ask him to present the program at that time. If you were definitely not interested, I would let this simmer a while longer. One point of timing is that if Syntex did approve the program next month, the new laboratory could be a running operation by September 1962, which should be a convenient time to start. (I should have stressed that Djerassi is one of the remarkable assets of the whole operation). Regardless of your personal interest, I would be pleased to have any comments or suggestions you would care to make. I would ask, however, that you keep the matter in confidence (as of course I would) until the discussion can be put on a formal basis.

I would appreciate hearing from you as soon as you feel able to reply You can call me at DAveport 1-2764 if you wish.

Best regards,

Joshua Lederberg